A STUDY OF POST-ISCHÆMIC PARÆSTHESIÆ

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Paræsthesiæ of the kind commonly known as "pins and needles" occur spontaneously in a variety of conditions. They may be produced deliberately by mechanical or electrical stimulation of a nerve, by overbreathing, or by cutting off the circulation to a limb and then releasing it. The present study is mainly concerned with the paræsthesiæ which follow a period of circulatory arrest in a limb, and its object has been to differentiate the various types of sensation which occur in these circumstances, determining their site of origin and their peripheral and central nervous pathways.

Historical

Several authors have described the sensory phenomena which occur during and after compression of a nerve or a limb. Only recent writers made these paræsthesiæ the main subject of their study; in earlier work the sensations were noted during the course of investigations on other problems of human physiology. Goldscheider (1886), while investigating temperature sense, noticed the paræsthesiæ which followed the release of local pressure on nerve trunks. He described these paræsthesiæ carefully, and they appear to be similar to those following release of the circulation to a limb. Ebbecke (1922) made detailed studies of the sensations resulting from electrical stimulation of nerves. He also wrote of the paræsthesiæ ("Nervenschwirren") produced by other methods, including those felt during recovery from pressure paralysis, and at the onset of anæsthesia caused by the intraneural injection of a local anæsthetic; he was clearly of the opinion that all these forms of paræsthesiæ were alike. Bourguignon and Laugier (1923), in studies of chronaxie, described two forms of paræsthesiæ, those occurring during a period of circulatory arrest in a limb, and those occurring after release of the circulation. Again, Lewis and

Grant (1925), while investigating reactive hyperæmia, noted that intense tingling and sometimes painful cramp occurred soon after restoration of the circulation to an ischæmic limb. Reid (1931), during experiments on muscular reactions following ischæmia of a limb, noted the sensations which occurred at the same time. He was of the opinion that they were caused by the restoration of circulation and arose in the sensory end-organs. Bazett and McGlone (1929, 1932), having extensively investigated the thermal sensations which follow release of the circulation, concluded that they were true paræsthesiæ originating in the appropriate end-organs rather than in the nerve trunks. In their studies they made observations on the "tingling" and "cramp" sensations which they at first believed arose from the end-organs; later, they expressed agreement with the following views of Lewis, Pickering, and Rothschild (1931). These authors investigated ischæmic paralysis and anæsthesia. In the account of their studies, they included a note on the sensations which followed release of the circulation to a limb. They recognized two components to the sensation, "tingling" or "pricks," and "pseudo-cramp." They presented evidence to show that the nerve impulses responsible for the sensations arose in the segments of nerves actually compressed by the occluding cuff; they believed that it was the nerve fibres subserving the sense of touch which were concerned in the production of the tingling sensation, and that the nerves from muscle afferent end-organs were concerned in the production of "pseudo-cramp."

Zotterman (1933), in a study of sensory disturbances resulting from ischæmia, confirmed many of the findings of Lewis, Pickering, and Rothschild. Like them, he showed that these sensations arose in the proximal parts of the nerve trunks, but he thought, from the painful character of the sensations,

that they were an affair of pain-conducting fibres rather than those of touch. While studying accommodation in human nerves, Kugelberg (1944) included observations on two forms of paræsthesiæ occurring during and after the arrest of bloodflow to a limb. He related their appearance to concurrent changes in nerve excitability. The paræsthesiæ which occurred during ischæmia he called "tactile paræsthesia." The paræsthesia which followed release of the circulation he thought consisted of two components, both painful in character; the first, an "irradiating stinging sensation," he considered was conducted by fibres subserving pain sense, while the second, consisting of "innumerable well-localized short pricks," was of an uncertain nature but was conducted in fibres finer than those transmitting light touch. He based these conclusions largely on comparisons with similar, though not identical, sensations which resulted from the stimulation of nerves by other methods, notably by various forms of electrical current. Kugelberg also investigated the feeling of tension which followed release of the circulation, and its relation to the paræsthesiæ and the spasms found in tetany. More recently, Weddell and Sinclair (1947) investigated "compression tingling" and "release pricking," the sensory phenomena occurring, respectively, during and after the arrest of the circulation to a limb. They deduced that "compression tingling" arose as a result of changes in the nerves compressed by the occluding cuff. They considered, however, that "release pricking" resulted from the stimulation of pain nerve-endings by metabolites during their removal from the tissues on return of the circulation.

From a study of the literature it is clear that the sensation which follows release of the circulation is considered by many authors to consist of more than one component. It is also apparent that there is a lack of uniform terminology: words like "tingling" are used to describe differing sensations by different authors, and this makes comparison of their results difficult. Little more is to be gained by what Zotterman calls "introspective analysis" of these paræsthesiæ. It would seem to be difficult to draw conclusions concerning the nature and mechanism of various kinds of paræsthesiæ which feel subjectively the same, but which occur under differing circumstances or are induced in different ways; it becomes even more difficult to do so when the sensation is complex, and when one component of it can be separated from the others only by a mental effort.

Definitions

It is possible to induce the individual components of the paræsthesiæ separately by means of various measures to be described later. Having become familiar with these components in their isolated form, it is easy to recognize each of them in experiments in which they occur together.

The following definitions will be used in this study.

Ischæmic paræsthesiæ are those felt during the arrest of the circulation to a limb. Their most noticeable component is a soft, diffuse tingling, felt peripherally. This paræsthesia is transient, lasting only a few minutes however long the ischæmia lasts. It disappears on rubbing the skin in the area where it is felt, and it invariably goes immediately the circulation is restored.

Post-ischæmic paræsthesiæ are those which follow release of the circulation to a limb. They consist of at least four components: (1) thermal paræsthesiæ; (2) buzzing or tingling; (3) pricking; (4) pseudo-cramp or a feeling of tension.

With the exception of the thermal paræsthesiæ, all these sensations are felt peripherally. They appear fairly abruptly, allowing their time of onset to be stated to within a few seconds; their termination is less definite, for they fade gradually.

1. Thermal paræsthesiæ are the first to be felt on return of the circulation. They consist of changing sensations of warmth and cold, and often of indefinable feelings which may only be expressed as "temperature" of some kind. These paræsthesiæ have been studied extensively by Bazett and McGlone, and will be given no further consideration in this paper.

2. Buzzing or tingling is in most subjects the next sensation to be felt. It is often described by subjects as a vibrating sensation and is localized superficially. When it is at its height it may be momentarily increased by any stimulus which deforms the skin in the area where it is felt, but not by very light touches. Similar stimuli may also induce this sensation a few seconds before it is due to begin spontaneously. Some minutes later, when the buzzing or tingling is waning, the application of the same stimuli will cause it to disappear, at least temporarily.

3. Pricking, in many subjects, is the most easily induced of the post-ischæmic paræsthesiæ, since it may follow periods of ischæmia too brief to produce tingling or pseudo-cramp. When present with the other paræsthesiæ, it is usually the most noticeable sensation. It consists of a feeling of rapidly repeated, irregularly spaced, discrete, little pricks, less sharp and painful than the pinpricks employed in the clinical testing of sensation; they are felt superficially, in the skin. This paræsthesia, when

at its height, may be increased momentarily by firm pressure or by gross movements in the area where it is felt; such stimuli will also produce pricking some seconds before it is due to begin spontaneously.

4. Pseudo-cramp is the name given by Lewis, Pickering, and Rothschild to a feeling of tension felt in the hand, wrist, and forearm in experiments on the upper limb, or in the foot and calf in experiments on the lower limb. It is a sensation which gives the impression that the fingers and wrist are being strongly flexed. Active and passive movements of the fingers and wrist increase this sensation, which is felt only after prolonged periods of circulatory arrest. After even longer periods of ischæmia, this paræsthesia is followed by involuntary muscular contraction which actually produces flexion of the fingers and wrist.

The following typical experiment illustrates the order in which the paræsthesiæ appear, their mode of onset, and the time for which they may be expected to last.

Experiment 1.—A sphygmomanometer cuff 12 cm. wide was placed on the arm above the elbow. The arm was elevated to prevent venous congestion, and the pressure in the cuff quickly raised to 200 mm. of mercury and maintained at this level, which was above the systolic blood pressure. With the arm rested on a table, the following events were observed.

About two minutes after arrest of the circulation, a soft tingling sensation (ischæmic paræsthesia) was felt, beginning in the finger-tips and spreading to the palm and then to the wrist. This sensation increased slightly in intensity, reached its maximum in a minute, and then subsided, so that about five minutes after the onset of occlusion it was gone.

For the remainder of the period of circulatory arrest, no further paræsthesiæ were felt. Ischæmic paralysis and anæsthesia began to be obvious after fifteen minutes.

After thirty minutes the pressure in the cuff was released; the sensations which followed were the post-ischæmic paræsthesiæ. Two to three seconds after release, thermal paræsthesiæ were felt in the whole limb, although they were more marked in the hand. They continued for about forty seconds. During this time both anæsthesia and paralysis recovered completely. About fifty seconds after release, the first striking sensation was felt; it consisted of tingling in the fingers and palms. It rapidly increased in intensity and spread to the whole hand and wrist. At the same time the feeling of tension developed. About seventy seconds after release, at a time when

the tingling and pseudo-cramp were still increasing, pricking was felt. Like tingling, it was felt first in the fingers, particularly on their palmar aspects, and spread rapidly to the whole hand and wrist. Two minutes after release of the cuff the total result was a severe and complex combination of sensations. The paræsthesiæ continued strongly until about four minutes after release, by which time it was apparent that the feeling of tension had gone and that pricking had diminished. There remained a continuous tingling with an occasional pricking sensation. This gradually diminished, and finally stopped about fifteen minutes after release of the cuff.

The duration of the post-ischæmic paræsthesiæ in this experiment are represented in Fig. 1. The paræsthesiæ can be appreciated in this clear manner only after the subject has experienced them separ-
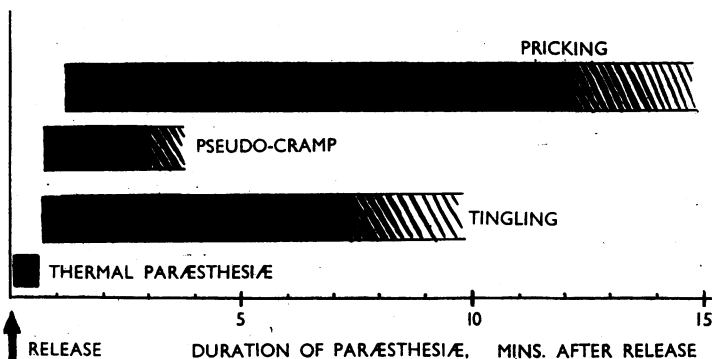

FIG. 1.—Diagram of the onset and duration of paræsthesiæ following arrest of the circulation for thirty minutes with a cuff above the elbow.

ately; experience plays a part in the ability to distinguish the various components of the combined sensation. The methods of separating the various components will be described later.

This experiment produces slightly different results in different individuals. The precise times of onset of the paræsthesiæ, their duration, and their relative intensity differ from subject to subject, although these factors remain fairly constant over a period of several years in a given subject.

Factors which Modify Post-ischæmic Paræsthesiæ

By altering the procedure given in Experiment 1, differences in the resulting sensations may be observed. The results so obtained will serve as evidence for conclusions relating to the differentiation, the site of origin, and conduction of the paræsthesiæ. An account, here, of the main factors producing these modified results will illustrate certain general characteristics of the paræsthesiæ.

The duration for which the limb is rendered ischæmic is the most important factor in determining the character, distribution, and duration of the paræsthesiæ. Subject to individual variations, it has been found that about five minutes is the minimum period of ischæmia in the arm to be followed by paræsthesiæ. The longer the occlusion, the more severe and more prolonged are the resulting sensations. After short occlusions, tingling and pricking are the only paræsthesiæ experienced, and they are restricted to the fingers and hand; after longer periods the area involved spreads to include the wrist and then the forearm. At least twenty minutes of ischæmia is required for pseudo-cramp to be felt. Whatever the period of ischæmia, there is always a delay of at least fifty seconds
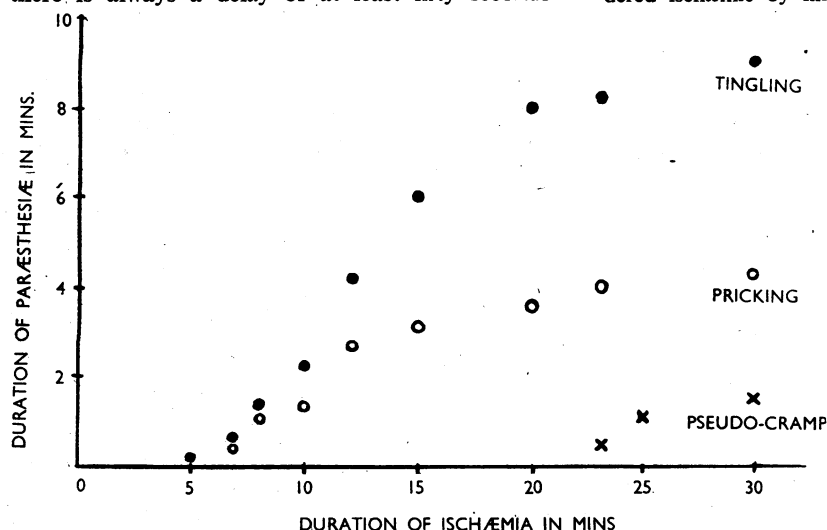

FIG. 2.—Graph showing the duration of paræsthesiæ following various periods of ischæmia. Single cuff above the elbow. (P.W.N.)

following release before the paræsthesiæ, other than thermal, are felt. Fig. 2 illustrates the duration of the paræsthesiæ after different periods of ischæmia; the figures recorded are the averages of many observations made in one subject over the course of two years. In our experiments, duration is selected as being the most easily measured property of paræsthesiæ. Any assessment of intensity in different experiments is too difficult to be of value, although, as a general rule, the more intense the paræsthesiæ, the longer do they last. Observations on intensity may be of value when events occurring simultaneously in the two hands are being compared. The area in which tingling and pricking are felt can usually be mapped out without difficulty. It covers the palmar surfaces of the hand and digits in the upper limb, or the plantar surface of the foot in the

lower limb after any period of ischæmia lasting less than twenty minutes; after longer periods of ischæmia the paræsthesiæ may be felt in and proximal to the wrist or ankle, but the area involved is not directly proportional to the duration of ischæmia. Occlusions of five and of twenty minutes' duration cause paræsthesiæ felt in exactly the same area; the only difference is one of intensity.

In the experiment previously described the circulation in the arm was allowed to continue unimpeded after release of the cuff. If the returned circulation is cut short by re-inflating the cuff the paræsthesiæ are reduced or even suppressed altogether, as the following experiment shows.

Experiment 2. (W.R.M.).—Both arms were rendered ischæmic by inflating cuffs placed above the elbows; after eight minutes the pressure in the cuffs was released. In the right arm the circulation was again arrested after fifteen seconds; the sensations felt in the two hands were then compared. In the left hand paræsthesiæ (tingling and pricking) began one minute after release and continued for four minutes. In the right hand no paræsthesiæ were felt at all, except thermal paræsthesiæ.

It appears that the return of normal circulation for fifteen seconds is insufficient to produce paræsthesiæ. It is to be noted, however, that it is sufficient for some blood to reach the ischæmic tissues of the limb, as the following three facts show. First, reactive hyperæmia appears in the usual way and is obvious five seconds after release; secondly, thermal paræsthesiæ (which originate in peripheral end-organs) are felt after two seconds; and thirdly, ischæmic muscle pain, which may be induced by voluntary contraction just before release of the circulation, vanishes three seconds after release.

If, in Experiment 2, the circulation of the right arm is re-arrested after thirty seconds, then paræsthesiæ are felt, and begin, as in the left hand, one minute after release. Their duration, however, is rather shorter than in the left hand. As the circulation remains arrested throughout the whole time for which these paræsthesiæ are felt, the changes responsible for their production must therefore have been initiated during the thirty seconds of restored

circulation. A certain minimum period of normal circulation following ischæmia is accordingly necessary for the appearance of post-ischæmic paræsthesiæ.

It has been found that, if constant results are to be obtained, at least twenty-four hours must elapse between experiments on the same limb. This applies to all experiments in which the ischæmia lasts more than twenty minutes ; it is likely that shorter experiments may safely be repeated at shorter intervals. Perhaps the most noticeable change in the results of an experiment repeated after an hour is a diminution or even an absence of the ischæmic paræsthesia. But post-ischæmic paræsthesiæ are also modified, especially after repeated periods of ischæmia ; the pricking element is diminished, the times of onset of the various paræsthesiæ are delayed, and their total duration is reduced.

The position of the occluding cuff determines the amount of a limb which is rendered ischæmic, and which, on release of the cuff, recovers from ischæmia. The more proximally the cuff is placed, the more readily are all forms of post-ischæmic paræsthesiæ produced, for they occur after shorter periods of occlusion, are greater in intensity, and last longer.

The width of the occluding cuff is of no importance provided that the blood flow to the limb is completely arrested. When two adjacent cuffs (total width 24 cm.) are used together to produce ischæmia, and released together, the resulting paræsthesiæ are precisely the same as when only one cuff (12 cm. wide) is used at the same level. By altering the position of the distal cuff, while keeping the proximal cuff in the same position, release of the proximal cuff alone will restore the circulation to various lengths of limb. It will then be found that the longer the length of limb recovering from ischæmia, the more marked will be the paræsthesiæ. When the proximal cuff is placed on the limb so that it overlaps the distal cuff, the recovery of the short segment of limb from ischæmia is accompanied by minimal paræsthesiæ.

Lewis, Pickering, and Rothschild showed that when the distal cuff alone is released, the whole limb remains ischæmic, and no paræsthesiæ are felt. It is thus the return of the circulation, and not the release of the pressure as such, which causes the paræsthesiæ. Again, it is possible to show that it is the duration of ischæmia, and not the duration of compression which determines the intensity of the paræsthesiæ.

The upper of two adjacent cuffs is inflated on the arm ; ten minutes later the adjacent lower cuff is inflated and the upper cuff deflated. This release of the upper cuff is followed by restoration of the circulation only to a small proximal segment of the limb, with resulting mild paræsthesiæ in the hand. Five minutes later, when these have ceased, the lower cuff is released. The paræsthesiæ which follow are marked, and correspond in severity with those which normally follow fifteen minutes' ischæmia. It is the ischæmia in the distal part of the limb, of fifteen minutes' duration, which determines the severity of the paræsthesiæ, although the distal cuff has been compressing the limb for only five minutes.

It is important that the pressure in the cuff should be above systolic pressure ; increasing it by increments of 25, 50, or 100 mm. Hg above systolic pressure does not alter the character or duration of the paræsthesiæ. In experiments with a clamp, in which the circulation is arrested in 12 cm. segments of limb, leaving the rest of the limb with a normal circulation, as in Experiment 11, pressures as low as 70 mm. Hg are adequate for the production of paræsthesiæ. But the maintenance of pressures below systolic level in a single cuff soon leads to great congestion of the veins and tissues distally, and the sensations resulting from this tend to make observations on true post-ischæmic paræsthesiæ difficult. However, paræsthesiæ of short duration do result from the release of a single cuff inflated to a pressure of 70 mm. Hg.

Post-ischæmic paræsthesiæ may be modified by altering the temperature of the limb. Placing the limb in a water-bath at 10° C. 5 minutes before applying the cuff causes a marked diminution in the tingling paræsthesia, and accentuates pricking. Unless otherwise stated, the experiments described in this study have been carried out at room temperature, at which the results obtained show little variation.

The Differentiation of Post-ischæmic Paræsthesiæ

We have already described the four types of paræsthesiæ which together make up the complicated sensations felt after release of the circulation to a limb. In differentiating them, we are concerned chiefly with the distinction between tingling and pricking, because they are most easily and frequently confused, and because they usually occur together. Thermal paræsthesiæ and pseudo-cramp are more distinct sensations, and consequently more readily recognized.

Thermal paræsthesiæ occur immediately after release, and end before other sensations are felt. In clinical cases in which temperature sense is lost in a limb, all forms of post-ischæmic paræsthesiæ may be induced in that limb except thermal paræsthesiæ (see Cases 4, 6, 7, and 8).

The sensation of *pseudo-cramp* also has a distinctive character. This paræsthesia commonly

occurs when other sensations are at their height; it is of some importance, therefore, to know that it may be felt by itself.

Experiment 3. (W.R.M.).—With a cuff applied to the arm as in Experiment 1, the circulation was arrested for ten minutes and released for thirty seconds; this cycle was repeated several times. After the fifth or sixth short period of release, the post-ischæmic paræsthesiæ differed from those after the first. Pseudo-cramp became the most prominent sensation; it began spontaneously about seventy seconds after release, lasted about a minute, and was then followed by very slight tingling and later by pricking. When the pseudo-cramp was present alone, tingling could be induced by touching the ventral surfaces of the fingers or hand, but if no such stimuli were applied the only sensation was a marked feeling of tension in the fingers, hand, and wrist.

By a suitable arrangement the radial nerve alone may be compressed in the arm. Release of the pressure on this nerve often results in a sensation of pseudo-cramp alone without the other forms of paræsthesiæ.

Experiment 4. (P.W.N.).—The forearm was rested on a padded table at shoulder height. A strap 5·5 cm. wide was placed over the arm 5 cm. above the lateral epicondyle, and the ends weighted with a 5-kg. weight. After twenty-five minutes there was hypoæsthesia in the skin of the distribution of the superficial radial nerve, and weakness of the extensors of the thumb. The pressure was released after thirty minutes. Seventy seconds later pseudo-cramp was felt in the radial side of the wrist; it spread up over the back of the forearm, and when at its height, ten seconds later, was accompanied by involuntary contraction of the extensors of the wrist and thumb. The feeling of tension lasted a minute in all; no other paræsthesia occurred spontaneously, but tingling could be induced by touching the skin in the area supplied by the radial nerve.

Again, as Bazett and McGlone (1931) have pointed out, pseudo-cramp becomes the most prominent of the paræsthesiæ felt after an adequate period of ischæmia in a limb which has been immersed in water at 45° C. Other forms of paræsthesiæ are not correspondingly increased.

These experiments confirm that pseudo-cramp is a distinct form of post-ischæmic paræsthesia. It is to be noted that in Cases 8 and 9, referred to later, all paræsthesiæ except pseudo-cramp are felt in the limb in which position sense is absent.

The differentiation of *tingling and pricking* remains to be considered. It has already been stated that post-ischæmic sensations vary in different individuals. One form of variation is seen after minimal periods of circulatory arrest (five or ten minutes). In such experiments, some subjects feel

only pricking, while others feel only tingling; a few feel both sensations.*

In subject W.R.T., for example, eight minutes was the minimum period of arrest necessary to produce any post-ischæmic paræsthesiæ, with the cuff applied above the elbow. Arrest lasting from eight to fifteen minutes resulted in pricking alone. After occlusions lasting over fifteen minutes, tingling was added to pricking though pricking outlasted it by several minutes. Twenty-five minutes' arrest was necessary to produce pseudo-cramp as well. In subject J.C., on the other hand, tingling was the most easily produced sensation. Arrest lasting from eight to ten minutes resulted in tingling alone. Fifteen minutes produced tingling and pricking, and still longer occlusions were necessary to produce pseudo-cramp as well.

The effects of repeated periods of occlusions have been referred to. They illustrate further differences between the tingling and pricking components of post-ischæmic paræsthesiæ.

After the fifth or sixth release in Experiment 3, tingling assumed a latent form; at first it was produced to an intense degree by touching the fingers or hand, but it did not appear spontaneously until a few minutes after release, and then only to a very slight degree. In this experiment, there was, in fact, a period when intense tingling was the only paræsthesia which could be induced; its vibrating character was easily noted, and no element of pain or pricking was observed. Transient pricking followed tingling.

A further distinction between tingling and pricking may be drawn from the different ways in which they are modified by altering the temperature of the limb. Pricking is considerably increased, and may be felt by itself if the limb is cooled throughout an experiment; there is also a tendency, though not so marked, for tingling to be increased when the limb is warmed. These effects are well seen after periods of ischæmia too short to produce pseudo-cramp.

They can be observed in all subjects; two examples are given, one in a subject in whom tingling normally outlasts pricking, and the other in a subject in whom pricking is usually the more prolonged paræsthesia.

Experiment 5. (P.W.N.).—Cuffs were applied to both forearms just below the elbows. The left forearm was immersed in a water-bath maintained at 40° C.,

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* The problem of identifying the sensation which a subject feels has been given much attention. Paræsthesiæ are subjective. In the last instance, therefore, there is no way of proving what it is a particular subject feels. However, in the great majority of over thirty subjects examined by us it has been possible to identify with reasonable certainty the type of post-ischæmic paræsthesia being felt. The peripheral distribution of the sensation, its time of onset, the kind of procedure being employed to induce it, and the effect of stimuli on it, have all been of value in confirming the type of sensation suggested by the subject's own description of it.

and the right in a water-bath at 15° C. throughout the experiment. Both cuffs were inflated five minutes after immersion, and released after twenty minutes' ischaemia. Post-ischaemic paræsthesiæ were felt as follows :

Left arm (warm)	*Right arm (cold)*
Tingling began 55 secs. after release and lasted 185 secs.	Tingling began 85 secs. after release and lasted 65 secs.
Pricking began 85 secs. after release and lasted 55 secs.	Pricking began 90 secs. after release and lasted 240 secs.

Pricking, therefore was present alone in the cooled right hand for 3 minutes, while tingling outlasted pricking in the warmed left hand.

Further, in this subject (P.W.N.), ischaemia of only seven minutes' duration at 10° C. produced pricking but no tingling, whereas similar occlusions at room temperature invariably gave tingling alone.

Experiment 6. (W.R.M.).—The conditions of the experiment were as in Experiment 5. Post-ischaemic paræsthesiæ resulted as follows :

Left arm (warm)	*Right arm (cold)*
Tingling began 70 secs. after release and lasted 280 secs.	Tingling began 80 secs. after release and lasted 220 secs.
Pricking began 40 secs. after release and lasted 110 secs.	Pricking began 65 secs. after release and lasted 540 secs.

Here again, pricking outlasted tingling in the cooled right hand, while tingling was more prolonged in the left. In this subject, short periods of ischaemia at room temperature invariably gave pricking alone, whereas short periods of ischaemia at 40° C. give tingling alone.

The results of Experiments 5 and 6 are illustrated diagrammatically in Fig. 3.

One may conclude from these experiments that, although tingling and pricking usually occur together, they are two distinct forms of post-ischaemic paræsthesiæ.

The Site of Origin of the Paræsthesiæ

In discussing the origin of the nerve impulses felt as post-ischaemic paræsthesiæ, the sensory pathway may be divided into three parts : the end-organs, the nerves distal to the cuff, and the nerves directly beneath the cuff. The part each plays in the production of paræsthesiæ is demonstrated by means of experiments now to be described.

There is ample evidence to show that sensory end-organs are not essential for the production of post-ischaemic paræsthesiæ. In the first place, paræsthesiæ may be induced in a subject with an amputation provided there is no damage or degeneration of the nerve trunks at the level of the cuff ; the paræsthesiæ are felt in the phantom hand or foot, and have their usual characteristics.[*]

Case 1.—Pte. F., a sniper, was wounded in the left forearm in July, 1944, and had an amputation through the lower forearm three weeks later. He was examined in March, 1947. A cuff was placed above the left elbow, 38 cm. above the stump, and inflated for twenty-five minutes. After this was released he felt tingling and pricking starting in the fingers and back of the phantom hand, and later a feeling as though the wrist was being forced into flexion. Tingling lasted six minutes, pricking about four minutes, and the feeling of flexion just over three minutes. After release of a similar length (38 cm. measured from the finger-tips) of the right arm, paræsthesiæ of the same type, but of slightly longer duration, were felt.

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[*] The common practice of dividing large nerve trunks as high as possible and crushing them during amputations makes it difficult to judge the level at which functioning nerve fibres end. It is certain that this level is often several inches above the stump, and it is therefore not surprising that paræsthesiæ frequently cannot be induced in such cases by compression with a cuff. The fact that they can be induced in some cases, however, is all that is relevant to the present argument.
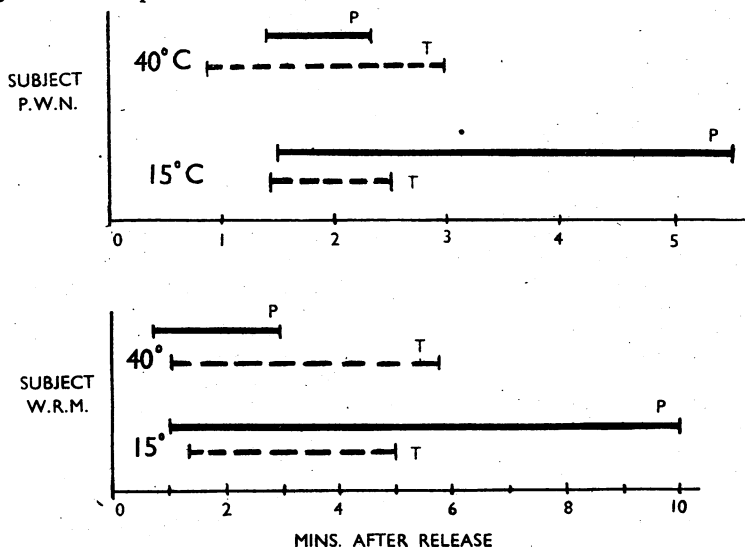

FIG. 3.—Diagram illustrating the effect of temperature on the duration of tingling (T) and pricking (P) in two subjects. (Cuffs below the elbows ; twenty minutes' ischaemia).

Paræsthesiæ may also be induced in the anæsthetic area in subjects with a complete peripheral nerve lesion provided the occluding cuff is placed above the lesion.

Case 2.—A patient had a complete lesion of his left median nerve just proximal to the wrist. At operation the injured segment of the nerve was resected and the ends re-sutured. At the time of the experiment, four weeks later, there was no sign of recovery ; Tinel's sign was negative. Cuffs were placed above the elbows and inflated for fifteen minutes. After release, paræsthesiæ were felt concurrently in both hands ; no difference was detected by the subject between the paræsthesiæ in the median and those in the ulnar areas of the affected hand.

In this case, the median sensory end-organs had no functional connexion with the central nervous system. Comparable results have been obtained in two other patients with complete ulnar nerve lesions at the wrist. These findings have been supported by inducing post-ischæmic paræsthesiæ when the nerves from the areas in which the paræsthesiæ are felt have been completely blocked by local anæsthetic distal to the occluding cuff. The following experiment illustrates this.

Experiment 7. (P.W.N.).—Procaine hydrochloride was injected into the median and ulnar nerves just above the wrist, producing a complete median and ulnar block. A cuff was then placed above the elbow and inflated for thirty minutes. After release, all three paræsthesiæ (tingling, pricking, and pseudo-cramp) were felt in the hand, thumb, and fingers, although these areas remained anæsthetic throughout the experiment and for some hours afterwards.

The following experiment excludes the cutaneous end-organs from taking part in the changes which result from release of the circulation, and demonstrates again that paræsthesiæ may occur without the participation of these end-organs.

Experiment 8.—One hand was immersed for a few seconds in a solution of 8 per cent. celloidin in equal parts of ether and alcohol. On withdrawal, the hand and fingers were coated with a thin transparent layer of celloidin which slowly contracted as it dried, so that after about fifteen minutes the fingers and much of the palm and dorsum of the hand developed an intense pallor resulting from ischæmia of the skin and subjacent tissues. Both hands were immersed in a water-bath at about 30° C. to equalize their temperatures, and cuffs were then inflated above both elbows. After twenty minutes the cuffs were released. The circulation was rapidly restored to the whole of the control limb, but in the hand coated with celloidin the fingers and most of the hand remained completely blanched and showed no sign of a return of circulation. In spite of this gross difference, paræsthesiæ of simultaneous onset and of equal intensity and duration were felt in the two hands.

The experiments just described (Cases 1 and 2, and Experiments 7 and 8) demonstrate clearly that the three forms of paræsthesiæ may all be induced without difficulty under conditions in which sensory end-organs can play no part. In these experiments the impulses felt as paræsthesiæ must, therefore, have arisen in the nerves. It does not necessarily follow that the end-organs contribute nothing to the sensations resulting from recovery of the circulation to the whole limb. The results of Experiment 8 do suggest that their contribution, if anything, is a small one ; there is no detectable difference between the paræsthesiæ resulting from release of the upper limb when the hand is included, and when it is not. More direct evidence on this point is provided by a further experiment with celloidin, in which the cutaneous end-organs of the hand are rendered ischæmic without involving significant stretches of nerves at the same time. Under these conditions, it may be shown that recovery of the skin from prolonged ischæmia does not produce paræsthesiæ.

Experiment 9.—The hand and fingers were coated with celloidin as described in Experiment 8. After the ischæmia produced by this method had continued for forty minutes the celloidin was rapidly removed by immersing the hand in a vessel of solvent ; within twenty seconds normal colour returned to the fingers and hand, but this recovery from ischæmia did not result in the appearance of paræsthesiæ.

In another experiment the celloidin coat was quickly dissolved from the tip of one of the constricted fingers ; a prompt return of the circulation to the finger-tip showed that the main digital arteries were not occluded by the pressure of the celloidin. It was probable, therefore, that only the most superficial of the sensory structures in the finger, that is, the cutaneous end-organs, were involved in this marked visible ischæmia.

Paræsthesiæ may also be felt after release of a cuff placed on the proximal part of a limb, even though the circulation remains arrested to the distal areas in which the paræsthesiæ are felt. Under these conditions the relevant sensory end-organs can play no part in producing sensations due to the returning circulation.

Experiment 10. (W.R.M.).—Cuff A was placed with its lower edge 5 cm. above the wrist, cuff B was placed as high as possible on the same arm, and both were inflated. After thirty minutes cuff B was released. Tingling, pricking, and pseudo-cramp were felt in the fingers, hand, and wrist, although these parts remained ischæmic for as long as cuff A was allowed to remain inflated.

It may be concluded that in this experiment tingling and pricking were not caused by events

taking place in the hand or fingers. The case of pseudo-cramp, however, demands special consideration, for it might be argued that this sensation, although referred distally, could arise in the deep structures of the forearm, for example in muscles which normally produce movements of the fingers and wrist. The following experiment shows that muscle afferent end-organs do not play an essential part in the production of the feeling of tension.

Experiment 11. (W.R.M.).—Cuff A was placed on the elbow and cuff B as high as possible on the same arm. Both cuffs were inflated. When cuff B was released after thirty minutes' ischæmia, the first and most severe paræsthesia was pseudo-cramp in the wrist and hand ; other paræsthesiæ were also felt. The limb remained ischæmic distal to the elbow.

In this experiment it is assumed that between the two cuffs there were no muscle afferent end-organs capable of causing sensations felt in the wrist or hand.

It may be concluded from these experiments that sensory end-organs are not the site of origin of impulses felt as post-ischæmic paræsthesiæ. Experiments may also be devised which show that the nerves distal to the occluding cuff are not essential for the production of post-ischæmic paræsthesiæ. Some of these experiments were described by Lewis, Pickering, and Rothschild ; the conclusions these authors drew from their results will be discussed later. Experiment 11 may be modified so that the two cuffs are adjacent. Release of the upper cuff now restores the circulation only to segments of the nerves directly beneath it, the nerves distal to it remaining ischæmic. Paræsthesiæ, nevertheless, do result, although they are less severe and of shorter duration than those resulting from the return of the circulation to the whole limb. As usual, they are felt in the hand and fingers. The following is an example of such an experiment.

Experiment 12. (M.S.).—Two cuffs were inflated adjacent to each other, above the left elbow. After twenty minutes the upper cuff alone was released, thereby restoring the circulation to a segment of arm 12 cm. long. Paræsthesiæ of the following duration were felt in the hand :

Tingling :   Onset 130 secs. after release ;
      Duration 6 mins.

Pricking :   Onset 90 secs. after release ;
      Duration 3 mins.

Pseudo-cramp : Onset 150 secs. after release ;
      Duration about 5 secs.

A control experiment, performed by releasing the circulation to the whole of the right arm, resulted

in paræsthesiæ of slightly more rapid onset, of much greater intensity, and of longer duration :

Tingling :   Onset 80 secs. after release ;
      Duration over 8 mins.

Pricking :   Onset 50 secs. after release ;
      Duration 6 mins.

Pseudo-cramp : Onset 70 secs. after release ;
      Duration 2 mins.

That post-ischæmic paræsthesiæ may be induced by local compression and release of short segments of limb was also shown by Lewis, Pickering, and Rothschild, by means of a special clamp. Briefly, the clamp is an apparatus with which short lengths of some of the main nerves in the arm can be compressed without stopping the circulation to the distal part of the limb. These authors showed that paræsthesiæ, felt in the hand, followed the release of pressure with this clamp. The following experiment compares the duration of paræsthesiæ induced by cuff and by clamp.

Experiment 13. (P.W.N.).—A clamp 12 cm. wide was applied to one arm above the elbow, and a cuff was placed on the other arm at the same level. Both were inflated for twenty-five minutes and then released simultaneously. Paræsthesiæ of the following duration were felt :

	Clamp	Cuff
Pseudo-cramp :	30 secs.	80 secs.
Pricking :	115 secs.	270 secs.
Tingling :	190 secs.	over 720 secs.

The sensations were much less severe on the side of the clamp.

As a rule, both the median and ulnar nerves are compressed when the clamp is applied above the elbow ; after release, paræsthesiæ are felt in the corresponding areas of the hand. If, in a particular subject or experiment, only the median nerve is compressed, as judged by the distribution of the resulting anæsthesia, then the post-ischæmic paræsthesiæ are confined to the median area of the hand.

It can be shown in the following manner that only those parts directly compressed by the clamp are rendered ischæmic by it, and that the nerves distal to it are unaffected.

Experiment 14. (W.R.T.).—The clamp was applied to the arm and inflated to 70 mm. Hg. for twenty minutes, by which time there was marked hypoæsthesia in the finger-tips. A cuff placed immediately distal to the clamp was then inflated, and a control cuff was simultaneously inflated in a similar position on the other arm. The clamp was released, leaving the cuffs inflated ; the anæsthesia caused by the clamp quickly cleared up and there followed the usual paræsthesiæ resulting from its release. In the course of the ensuing twenty minutes, anæsthesia due to the

cuffs developed in both hands at exactly the same rate. Moreover, after their release at the end of this time, paræsthesiæ of the same intensity, type, and duration were then felt in the two hands.

We have here a clear indication that the nerves distal to the clamp had been unaffected by its application over a period of twenty minutes, and that they afterwards reacted in exactly the same way as those in the control limb.

By blocking the main nerves at the wrist, it can also be shown that the sensory end-organs in the hand play no part in the production of post-ischæmic paræsthesiæ resulting from release of the clamp.

Experiment 15. (P.W.N.).—The left median and ulnar nerves were injected with procaine and adrenaline 2 cm. above the wrist. Complete median and ulnar paralysis and anæsthesia followed. The clamp was applied to the arm and inflated to 70 mm. Hg. for twenty minutes, during which time the circulation in the hand remained apparently normal. After release of the clamp, paræsthesiæ of the following duration were felt in the anæsthetic hand and fingers.

Tingling :   Onset 65 secs. after release ;
              Duration 145 secs.

Pricking :   Onset 105 secs. after release ;
              Duration 125 secs.
              No pseudo-cramp was felt.

In experiments with the clamp, then, neither the sensory end-organs nor the nerves distal to the segment compressed contribute to the production of paræsthesiæ. Impulses felt as paræsthesiæ must, therefore, arise in the larger nerves directly beneath the clamp, when the circulation is restored to them.

By blocking the main nerves with local anæsthetic just distal to a cuff, all sensory effects resulting from return of the circulation to the distal parts of the limb can be excluded. Under such conditions, post-ischæmic paræsthesiæ are still felt ; it follows, therefore, that the impulses responsible for these sensations originate in the nerves directly underneath the cuff. In carrying out such an experiment, the cuff must be placed a sufficient distance above the point of injection to allow for the spread of local anæsthetic along the nerves. In early experiments, the median and ulnar nerves were blocked at the elbow and the cuff applied immediately above the points of injection ; release of the cuff was not followed by paræsthesiæ. Simple tests with an electrode suggested that there was an extensive spread of local anæsthetic up the nerve trunks, so that the cuff, applied about twenty minutes later, was in fact compressing anæsthetized nerve. For example, when 2 c.cm. of 2 per cent. procaine with adrenaline was injected into the ulnar nerve at the wrist, this nerve was soon found to have become anæsthetic to strong faradic stimulation for at least 8 cm. above the point of injection.

From the experiments described it would at first seem reasonable to conclude that impulses responsible for post-ischæmic paræsthesiæ arise in those parts of the nerves actually compressed by the cuff. There is adequate proof that they can be produced without sensory end-organs and without functioning nerve trunks distal to the compressed segment. But it is important to remember that in all these experiments the longer the length of nervous tissue recovering from ischæmia the more marked and more prolonged are the paræsthesiæ. These facts are shown diagrammatically in Fig. 4. It seems unlikely, therefore, that these impulses arise solely from beneath the cuff in experiments in which the circulation is restored to the whole limb.

In order to investigate this point, many experiments have been conducted comparing the duration of post-ischæmic paræsthesiæ resulting from the release of different lengths of nerve. Two methods have been employed. In the first, a single cuff was released at different levels in the arm and forearm, the length of nerve involved being estimated by measuring the distance from the upper edge of the cuff to the middle finger-tip. In the second, two cuffs were used, one placed high on the arm and the other at different distances below it ; release of the upper cuff thereby restored the circulation to different lengths of nerve. When the cuffs were adjacent, only 12 cm. (the width of a cuff) of nerve was released ; if the cuffs were separated, longer lengths of nerve had their circulation restored. Tables I and II give the results obtained by the two methods.

The effect of releasing less than 12 cm. of nerve can be studied by overlapping the cuffs or by the use of weighted bands or other hard objects which can be made to press on a single nerve. It has been found that when less than 2 cm. of a nerve is compressed, even for periods long enough to cause anæsthesia, release is never followed by paræsthesiæ.

It is seen that after a constant period of ischæmia release of the circulation results in paræsthesiæ which are more severe when a greater length of nerve is involved. Two explanations of this fact may be considered. First, all parts of the nervous pathway concerned may be capable of contributing more or less equally to the paræsthesiæ ; each part of the affected nerve would add its increment to the resulting sensations, so that a greater length of released nerve would produce a more marked result. Alternatively, the more proximal parts of the nerves might be more sensitive to return of the circulation ; the longer lengths of nerve necessarily include the more proximal parts and would therefore produce
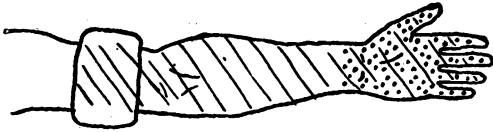
Release of single cuff above elbow restores circulation to whole limb and is followed by marked paræsthesiæ felt in the hand (Expt. 1).
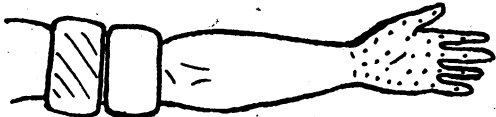
Amputation at wrist. Release of cuff is followed by paræsthesiæ in phantom hand (Case 1),
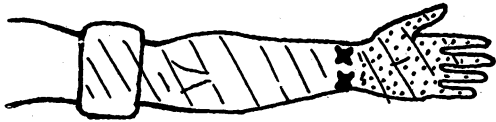
Complete nerve-block or nerve lesion at wrist. Release of single cuff is followed by paræsthesiæ felt in the hand (Case 2, Expt. 7).

Lower cuff at wrist remains inflated. Release of upper cuff is followed by paræsthesiæ felt in the hand (Expt. 10).

Lower cuff above elbow remains inflated. Release of upper cuff is followed by slight paræsthesiæ felt in the hand (Expt. 11).
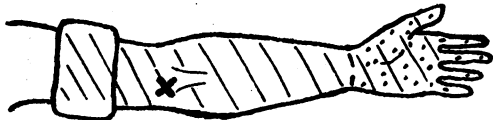
Complete nerve block at elbow. Release of cuff is followed by slight paræsthesiæ felt in the hand (page 10).

Clamp applied above elbow. Release is followed by slight paræsthesiæ felt in the hand (Expt. 13).

Areas to which the circulation is restored.

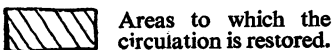Areas in which the paræsthesiæ are felt.

FIG. 4.—Diagram summarizing the results of experiments relating to the site of origin of impulses felt as paræsthesiæ.

more marked paræsthesiæ. The second hypothesis was that favoured by Lewis, Pickering, and Rothschild, but it is one which we are unable to confirm. In the first place, Table II shows results which clearly indicate that the inclusion of distal parts of the nerve adds considerably to the duration (and severity) of the paræsthesiæ. Again, the sensitivity of the nerves at different levels in the limb can be tested by further experiment.

TABLE I

DURATION OF PARÆSTHESIÆ FOLLOWING 40 MINUTES' ISCHÆMIA PRODUCED BY A SINGLE CUFF AT DIFFERENT LEVELS IN UPPER LIMB (P.W.N.).

Position of cuff, (cm., from middle finger-tip)	Average Duration of paræsthesiæ (secs.)		
	Tingling	Pricking	Pseudo-cramp
Upper arm (68 cm.)	930	510	120
Lower arm (63 cm.)	730	170	100
Upper forearm (49)	640	130	50
Lower forearm (33)	200	120	20

TABLE II

DURATION OF PARÆSTHESIÆ FOLLOWING RELEASE OF UPPER CUFF, WITH LOWER CUFF AT DIFFERENT DISTANCES BELOW IT (UPPER LIMB, 20 MINUTES' ISCHÆMIA) (W.R.M.).

Length of limb released (distance between upper edges of cuffs)	Average duration of paræsthesiæ (secs.)		
	Tingling	Pricking	Pseudo-cramp
63 cm. (whole limb) ..	690	480	80
29 cm. (hand excluded)	570	480	60
19 cm. ..	370	180	Nil
12 cm. (width of a cuff)	320	120	Nil

Experiment 16. (Consisting of several similar experiments).—Two cuffs were applied, adjacent to each other. In the different experiments the position of these two adjacent cuffs was varied, so that different parts of the limb were compressed. By releasing only the proximal cuff, the circulation was restored to stretches of nerve 12 cm. long at different levels. It was found that the release of such segments produced paræsthesiæ of fairly constant duration and severity, wherever the cuffs had been placed. Although the duration of paræsthesiæ in these experiments was not always the same, there was no constant tendency for the paræsthesiæ to last longer after releasing more proximal segments.

It may be concluded, then, that post-ischæmic paræsthesiæ result from recovery in all parts of a nerve, and that when the whole limb is recovering from ischæmia all parts of the nerve contribute to the resulting sensations. It must be admitted that these facts do not appear to apply to all the nerves in a limb. In experiments of moderate duration performed on the arm, tingling and pricking are invariably felt only in the palm of the hand and fingers, indicating that the median and ulnar nerves are chiefly involved. The recovery of considerable lengths of other sensory nerves (the cutaneous nerves of the forearm, for example) is not associated with paræsthesiæ felt in their areas of distribution. Yet, as we have seen, the recovery of quite short lengths of median and ulnar nerves at any level in the arm results in paræsthesiæ felt in the palm and fingers. Problems arising from these conflicting observations will be referred to again.

The Nerve Fibres Conducting the Paræsthesiæ

The results of experiments on different subjects have led us to believe that the impulses interpreted as the three paræsthesiæ, tingling, pricking, and pseudo-cramp, arise and are conducted in the nerve fibres normally concerned with the senses of touch, pressure, movement, and position. They are not conducted in sympathetic fibres, or in those concerned with the senses of pain, warmth, or cold. The evidence for these views follows.

With the special clamp already referred to, a progressive anæsthesia can be produced in the hand, resulting from local changes in the compressed nerve trunks ; the circulation to the arm and hand meanwhile remains undisturbed. Following the application of the clamp, different forms of sensation are lost in the fingers and hand at different rates, cold and pain being the last to go.* In a partial nerve block of this type, inflation and release of a cuff placed distal to the clamp will only cause paræsthesiæ if the nerve fibres conducting them remain unblocked. If the clamp has been in position too long, there will be complete loss of all forms of sensation in the hand at the time the cuff is released, and no paræsthesiæ will be felt. Similarly, by releasing the cuff when only pain and cold senses still remain in the hand, it can again be shown that no paræsthesiæ are felt. The following experiment is given in illustration.

Experiment 17. (W.R.T.).—A clamp was applied to the left arm. A cuff was applied just distal to it, and a control cuff placed on the right arm at the same level.

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* For detailed accounts of this progressive centripetal anæsthesia, the articles by Lewis, Pickering, and Rothschild (1931), and by Lewis and Pochin (1938) may be consulted.

0 *minutes*. Clamp inflated to 70 mm. Hg. Circulation at the wrist remained normal.

6 *minutes*. Both cuffs inflated to 200 mm. Hg.

26 *minutes*. Sensation tested in the left hand. From the wrist downwards there was complete loss of touch, pressure, and warmth senses ; position sense in the little finger was absent. There was no loss to pain sense as tested by pinprick, but this stimulus, when applied to the fingers, caused a delayed and unusually painful sensation which could not be localized. Cold sense was present in the palm but not in the fingers.

28 *minutes*. Both cuffs were released ; the clamp remained inflated. Reactive hyperæmia developed equally in both hands. Paræsthesiæ, lasting seven minutes in all, were felt in the right (control) hand. No paræsthesiæ were felt in the left hand.

35 *minutes*. Sensation again tested in the left hand. The only significant change from the previous test was that the area of modified pain sense had extended to the palm.

Fig. 5 illustrates this experiment, which shows that the paræsthesiæ did not arise or travel in the nerve fibres subserving the senses which remained in the left hand, that is, in cold or pain fibres.

By inflating the clamp and cuff together in this experiment, a nerve block results which is less complete by the time the cuff is released. Provided some tactile sense then remains in the hand, paræsthesiæ will be felt. These results have been confirmed on many occasions, but, using this method of producing a partial nerve block, we have not been able to establish a clearer relationship between the type of sensory loss and the form of paræsthesia which is blocked. For it has been our experience that the various forms of sensation (except for pain and cold) are lost so nearly simultaneously that prolonged observation at a chosen level of anæsthesia is difficult.

When a local anæsthetic is injected near a nerve trunk, there follows a partial nerve block which differs in certain important respects from that caused by the pressure of the clamp. Sympathetic and pain-conducting fibres are paralysed first, fibres subserving temperature senses next, and only later are those subserving touch affected. With care it is possible to induce partial anæsthesia which remains in the same state for several hours. Here again, compression and release of a cuff placed distal to such a nerve block will produce post-ischæmic paræsthesiæ in the area supplied by the nerve, only if those fibres conducting the paræsthesiæ are still functioning. The results of several experiments have shown that tingling, pricking, and pseudo-cramp may still be felt when sympathetic fibres are paralysed, and when pain, warmth, and cold senses are completely blocked.

Experiment 18. (W.R.M.).—Two per cent. procaine with adrenaline was injected near the median nerve just above the right elbow. A partial nerve block developed so that half an hour later the skin was hot and dry in the median area, and there was complete loss of pain (pinprick), warmth and cold, and light touch (cotton wool) ; heavier touches were felt. A cuff was inflated on the forearm just distal to the point of injection, and was released after fifteen minutes. The initial temperature paræsthesiæ were not felt in the median area, but subsequently tingling and pricking were both felt over the whole hand and lasted for five minutes. The only detectable difference between these paræsthesiæ in the median and ulnar areas was that the onset of pricking was slightly delayed in the median area. After the paræsthesiæ had subsided, sensation in the hand was again tested and found to be unchanged, apart from slight recovery of light tactile sense ; there was still a total pain, temperature, and sympathetic block in the median area. In this experiment, the period of circulatory arrest employed (fifteen minutes) was insufficient to induce pseudo-cramp. (This form of paræsthesia has been felt after longer periods of arrest distal to a similar nerve block.)

CLAMP

NO PARÆSTHESIÆ

Only painful stimuli felt

Pain and cold senses present

Normal sensation

CONTROL LIMB
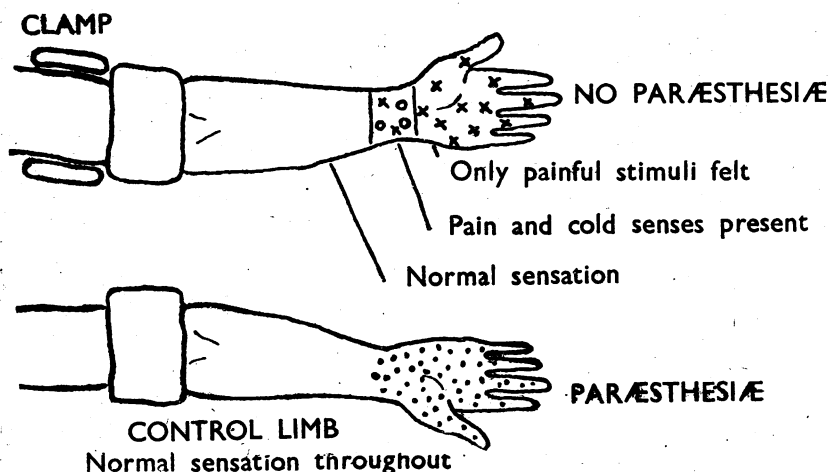Normal sensation throughout

PARÆSTHESIÆ

FIG. 5.—Diagram illustrating Experiment 17, in which a clamp maintains a partial nerve block and also stops the conduction of paræsthesiæ.

From the results obtained with these two methods of partial nerve block, certain types of nerve fibre can be excluded as possible pathways in which the paræsthesiæ are conducted. Clamp experiments show that post-ischæmic paræsthesiæ (except thermal paræsthesiæ) do not run in fibres subserving cold or pain; chemical block experiments show that these paræsthesiæ are not conducted in the fibres subserving pain, warmth, or cold, or in the sympathetic fibres.*

Lewis, Pickering, and Rothschild observed that when post-ischæmic paræsthesiæ were at their height, tactile stimuli applied to the affected areas increased the sensations, whereas other stimuli (temperature and pinprick) had no effect on them. They suggested, therefore, that the fibres subserving the sense of touch were also concerned in the production of the paræsthesiæ. We were able to confirm and extend their observations by studying the effect of stimuli on the various individual forms of paræsthesiæ.

The following methods of applying stimuli were employed.

Warmth was applied by radiant heat, using a modification of the instrument described by Stone and Dallenbach (1934). Cold stimuli were provided by the use of an ethyl chloride spray. Touch was applied with von Frey's hairs or with a wisp of cotton wool. Pressure was applied with a pencil, a pin's head, or observer's fingers. Painful stimuli were produced by pinprick. The initial effects of contact of the pin with skin were ignored, as pain was then complicated by stimulation of the tactile sense; further pressure with the pin gave a purer painful stimulus.

These stimuli were applied to the areas in which isolated forms of paræsthesiæ were being felt. Touch or movement sufficient to deform the skin increases the intensity of tingling. Considerable pressure which meets with firm resistance from the bones of the hand or fingers increases pricking. Active or passive movements of the fingers or wrist increase the feeling of tension. These stimuli also induce the corresponding paræsthesiæ under conditions already described in which the sensations are " latent " (see Experiment 3). Painful stimuli, warmth, cold, and very light tactile stimuli are all without effect on the paræsthesiæ.

The effects of certain stimuli on the areas on which paræsthesiæ are being felt may be tested in another manner. When a cuff applied to the arm arrests the circulation for about an hour, there is loss of all forms of sensation distally except that of pain. At this stage, a second cuff is applied just distal to the first, and the first cuff is released. A partial recovery of some forms of sensation occurs, and at the same time marked paræsthesiæ are felt in the hand. In effect, there is a partial nerve block distal to a stretch of nerve recovering from ischæmia. Areas can thus be prepared in which post-ischæmic paræsthesiæ are felt, but which are sensitive only to warmth, cold, or painful stimuli. These stimuli can be applied uncomplicated by any tactile or pressure stimulus; they are without effect on the paræsthesiæ, as the following experiment shows.

Experiment 19. (P.W.N.)—A cuff was applied above the elbow and inflated to 200 mm. Hg. An hour later the entire limb distal to the cuff was insensitive to all forms of stimuli except painful ones. A second cuff was inflated immediately below the first, which was then released. This produced the usual paræsthesiæ in the hand and wrist. While they were being felt, various stimuli were applied to the hand, but none had any effect on the paræsthesiæ; painful stimuli were the only ones to be felt. Ten minutes later the procedure was repeated; a third cuff was inflated just below the second, and the second cuff was released. Again the usual paræsthesiæ followed, and again the effect of stimuli on them was tested. In the lower forearm and wrist, skin-deforming touch, pressure, and movement increased the paræsthesiæ; stimulation everywhere distal to the wrist had no effect. In the forearm and wrist all forms of sensation had recovered, but distal to this, only pain, warmth, and cold were felt.

The interpretation of these results rests, of course, on the assumption that a paræsthesia which is increased by stimulation of a certain sense, is conducted in the nerve fibres normally concerned with that sense.

Evidence so far presented suggests, then, that the tingling element of post-ischæmic paræsthesiæ arises and is conducted in those fibres subserving touch (but not the lightest touch sensation induced by stroking with a hair), that pricking is conducted in those fibres subserving a sense of firm pressure, and that pseudo-cramp is conducted in those fibres subserving the sense of movement. By exclusion the evidence clearly shows that these three paræsthesiæ are not conducted in sympathetic fibres, or in those subserving the sensations of warmth, cold, and pain.

Additional proof that sympathetic fibres are not concerned can be provided in experiments on patients with sympathectomized limbs. In such patients, the usual post-ischæmic paræsthesiæ appear to be unaltered by interruption of the sympathetic pathways. The following case is an example.

Case 3.—A man aged 55 had suffered from symmetrical Raynaud's disease of his hands for six years. A right

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* In experiments involving a partial block with the clamp, the appreciation of painful stimuli has been accepted as evidence that pain sense is present; no attempt has been made to distinguish between ' first pain ' and ' delayed pain.' In the experiments with procaine block, pain sense as a whole is absent.

preganglionic cervical sympathectomy was performed. At the time of the experiment two weeks later there was complete sympathetic paralysis below the right elbow. Cuffs were applied to both arms and inflated for twenty minutes. Ischæmic paræsthesiæ, and, after release, post-ischæmic paræsthesiæ were felt in both hands ; no difference was noted between the sensations on the two sides, except that the moment of maximum intensity on the right side occurred earlier than on the left. The duration of post-ischæmic paræsthesiæ was four minutes on both sides.

The Central Nervous Pathways Conducting the Paræsthesiæ

Evidence relating to the pathways concerned in the conduction of post-ischæmic paræsthesiæ has been sought from experiments on patients with lesions of the central nervous system. Several patients have been examined in whom there has been interruption of tracts subserving pain and temperature. The simple experiment of occluding the circulation first to a normal limb was performed on these patients so that they could learn to distinguish the three paræsthesiæ. The forms of paræsthesiæ felt in the limb from which some sensory pathways are blocked depend on which tracts remain normal. Thus if a lesion blocks a tract in which the paræsthesiæ are not conducted, normal paræsthesiæ will be felt ; but if a lesion blocks a tract in which a paræsthesia is conducted, this paræsthesia will not be felt. The results conform with the findings already recorded, and show that post-ischæmic paræsthesiæ are not conducted in tracts subserving pain and temperature, but in those subserving touch and position senses. Evidence of a similar kind has been obtained suggesting that pseudo-cramp in particular is conducted in tracts concerned with the sensations of movement, position, and vibration.

Case 4.—A man, under the care of Sir Charles Symonds, had a thrombosis of the left posterior inferior cerebellar artery. At the time of the experiment, two months later, there was loss of appreciation of warmth, cold, and pain on the right limbs, and no sensory abnormality on the left limbs. Cuffs were placed above his elbows and inflated for thirty minutes. On release, the first sensation, one of heat, which was felt on the normal left hand, was not felt on the right ; otherwise all paræsthesiæ (tingling, pricking, and pseudo-cramp) were felt equally on the two sides.

Case 5.—A man under the care of Dr. E. A. Carmichael had a thrombosis of the left posterior inferior cerebellar artery. Three months later the sense of pain, which was tested by pinprick or by squeezing the muscles, and the senses of warmth and cold were absent in the right limbs, although the senses of touch, position, movement, and vibration were all present ; all forms of sensation were normal in the left limbs. Cuffs were

placed above the knees and inflated for thirteen minutes. On release, tingling and pricking were felt in both feet, although they lasted longer in the left. Again, cuffs were placed above the elbows and inflated for thirty minutes ; after release, tingling, pricking, and " gripping cramp " were felt in both hands, although for a short time they were more marked on the left.

Case 6.—A woman, under the care of Sir Charles Symonds, suffering from syringomyelia, had complete loss of pain and temperature sense over the right side of her face, right arm, and right trunk down to the level of the ninth dorsal segment ; she had no other sensory loss. Cuffs were placed above the elbows and inflated for thirty minutes. After release she felt the initial thermal paræsthesiæ only on the left side ; she felt all the other paræsthesiæ in both hands, and was unable to detect any difference between the sensations on the two sides.

Case 7.—A man had a bilateral upper dorsal cordotomy performed for painful tuberculous cystitis. Six weeks later, it was apparent that the interruption of the pain and thermal pathways was complete only on one side. In the left lower limb there was complete loss of pain, warmth, and cold sense ; there was no loss of tactile, vibration, movement, or position senses ; in the right lower limb there was slight loss of pain sense of uneven distribution, but thermal, tactile, movement, and position senses remained normal. Cuffs were applied above both knees and inflated for thirty minutes. After release, pricking and tingling were felt in both feet. There was an initial " hot feeling " on the right side, which was not noticed on the left. Pricking started and ended at the same time, and was of equal intensity on the two sides ; tingling was of the same intensity, but lasted one minute longer on the right (eleven minutes).

In spite of complete interruption of the pain and thermal pathways on one side, all these four subjects felt the usual paræsthesiæ (tingling, pricking, and pseudo-cramp) in the affected limbs ; it may be concluded, therefore, that the impulses giving rise to these sensations travel in the remaining intact sensory tracts, that is, in the posterior columns of the cord.

The following cases provide evidence relating to the conduction of the impulses felt as pseudo-cramp.

Case 8.—A man, under the care of Dr. E. A. Carmichael, had suffered an injury to his spinal cord at the level of the eleventh dorsal segment, which had caused a Brown-Séquard syndrome. Over the whole of his left lower limb he had complete loss of the sensations of pain and temperature ; touches with cotton wool were not always appreciated, but the senses of position and movement were normal. In his right lower limb he had loss of the senses of position and movement in all toe and ankle joints, and over the entire limb there was loss of vibration sense ; other senses were normal. Cuffs were placed on his thighs and inflated for thirty minutes.

After release, the following paræsthesiæ were felt :

Left	Right
(Pain and temperature absent)	(Position sense absent)
No thermal paræsthesiæ.	Feeling of heat.
Feeling of tension.	No feeling of tension.

Tingling and pricking were felt on both sides, but lasted slightly longer on the right.

It is to be noted that there was no feeling of tension on the side in which there was gross impairment of position, movement, and vibration senses, but that tingling and pricking were felt on both sides. Interruption of the pain and temperature pathways suppressed only the initial temperature paræsthesiæ.

Case 9.—A young doctor suffered from disseminated sclerosis. In both his upper limbs there was complete absence of vibration sense, and there was some loss of position sense in the fingers. Tactile sense was normal when tested with cotton wool, although very slight diminution could be demonstrated with von Frey's hairs. Pain and thermal senses were normal. Cuffs were applied above both elbows and inflated for thirty minutes. After release, tingling and pricking were felt to a marked degree in both hands. There was no feeling of tension on either side.

In this case, pseudo-cramp was the only paræsthesia which was not felt ; this was associated with a lesion blocking the pathway which normally conducts the sensation of vibration and the sense of position of the fingers.

Discussion

Experimental evidence has been presented which shows that the impulses felt as post-ischæmic tingling, pricking, and pseudo-cramp arise in the larger nerves of a limb. Reid (1931) and, more recently, Weddell and Sinclair (1947) concluded from their investigations that post-ischæmic pricking did not arise in the nerves but in certain peripheral nerve-endings. Such a deduction does not appear to be valid in the light of the experimental results obtained in patients with amputated limbs and with peripheral nerve lesions (Cases 1 and 2), for in such experiments peripheral nerve-endings were clearly incapable of contributing to any of the forms of paræsthesiæ.* Moreover, in the experiment with celloidin (Experiment 9), ischæmia of the fingers and hand which, it may be assumed, involved only

the end-organs, was not followed by any form of paræsthesiæ.

It has been shown that post-ischæmic paræsthesiæ are more severe when longer lengths of limbs are released ; it is believed that this is because all parts of the larger nerves in a limb, except the nerve-endings, appear to be the site of origin of impulses felt as paræsthesiæ. In this respect, our findings have not confirmed the suggestions of Lewis, Pickering, and Rothschild, who stated that changes in the most proximal part of the nerves are largely responsible for the sensations. These authors considered that the sensations following release of the circulation showed certain resemblances to the centripetal anæsthesia which develops during ischæmia in a limb. For example, they found that the region of a nerve in which conduction is most depressed during ischæmia is the most proximal part (beneath the cuff). The state of this segment of nerve alone therefore determines the degree of anæsthesia observed ; lesser degrees of block present in more distal parts of the nerve are of no consequence. On the same basis, they believed that the most proximal part of the nerve is likewise the most sensitive to a return of the circulation, and is therefore the site of origin of the paræsthesiæ. It must be pointed out that, although the proximal segment of a nerve is one of the places where impulses arise spontaneously, this segment of nerve is still capable of conducting impulses felt as paræsthesiæ which arise distal to it. In fact, all parts of the nerve may contribute to the resulting sensation.

Another difference between post-ischæmic paræsthesiæ and centripetal anæsthesia is important. Contrary to the accounts of many writers, the area in which the paræsthesiæ are felt does not increase in a strictly centripetal fashion as the duration of ischæmia is increased. In short experiments on the upper limb, for example, tingling or pricking is not confined to the finger-tips, but may involve any part of the palmar surface of the hand or fingers. Even in very brief experiments resulting in fleeting and barely perceptible paræsthesiæ, the sensations are usually felt scattered all over the median and ulnar areas. In longer experiments the sensations are increased in intensity, but they still remain confined to the same areas ; it is only after prolonged arrest that the paræsthesiæ may spread to involve the forearm. It is difficult to account for this relatively constant distribution of the paræsthesiæ by a greater sensitivity of longer nerve fibres to a return of the circulation, as suggested by Lewis, Pickering, and Rothschild. Further, such an hypothesis does not account for two conflicting facts already commented on : first, that release of the

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* Weddell and Sinclair were unable to induce " release pricking " in two amputation cases. One possible reason for the failure of some amputation cases to exhibit post-ischæmic paræsthesiæ has already been given ; thus, out of seven such cases examined by us, post-ischæmic pricking was obtained in two.

circulation to the whole limb does not normally produce paræsthesiæ in areas of the forearm supplied by long cutaneous nerves, and secondly, that release of very short lengths of median or ulnar nerves results in paræsthesiæ in the areas supplied by them. These apparently incompatible results may perhaps be best explained on the basis of a peculiar sensitivity of the larger peripheral nerves (e.g. median, ulnar, radial) to a return of the circulation. Some property of a large nerve as such, appears to determine the reactions of its component nerve fibres. Paræsthesiæ are felt in the palm, not because the sensory fibres leading from the palm are long, but rather because they are contained in one of the largest nerves in the arm. Why the large nerves should react so characteristically to arrest and return of the circulation is not at present clear.

Results already given suggest that each form of paræsthesia is related to a particular form of peripheral sensation ; tingling to the sensation of touch, pricking to the sensation of pressure, and pseudo-cramp to the sense of movement and position. The paræsthesiæ may be modified, each to a different extent, by changes in the temperature of the whole limb, by repeated circulatory arrest, and occasionally by deliberate partial nerve block, which procedures are known to affect the conduction in sensory fibres to varying degrees. There is some physiological basis, then, for the supposition that tingling, pricking, and pseudo-cramp are distinct phenomena associated with different sensory nerve fibres. The prominence of pseudo-cramp after release of the radial nerve may be due to the presence in this nerve of a high proportion of fibres subserving position sense, and a correspondingly small number of cutaneous afferent fibres. Several authors have noted the unpleasant and painful character of post-ischæmic paræsthesiæ, and particularly of the pricking element ; a few, Zotterman, Kugelberg, and Weddell and Sinclair, have been led to believe that this sensation results from impulses travelling in pain-conducting nerve fibres. But the fact that all paræsthesiæ may still be induced when the pain, thermal, and sympathetic pathways have been blocked, excludes the possibility of their origin or conduction in any of these pathways. There seems, in fact, to be no paræsthesia associated with pain sense in the post-ischæmic period. Nor is there any evidence to suggest activity of the sympathetic nerve fibres ; vasoconstriction, sweating, and erection of the hairs have not been observed after release of the circulation. It is to be noted that sympathetic nerve fibres, and those concerned in the conduction of impulses felt as pain, are both of small diameter and non-medullated, and are known to be relatively resistant to the effects of asphyxia.

In this study no attempt has been made to account for the mechanism underlying the production of post-ischæmic paræsthesiæ ; investigations relating to this problem are still being conducted. That the effect is primarily a vascular one has been suggested by Lewis and his associates, and has been confirmed in experiments recorded here. It has been shown that an adequate period of ischæmia must be followed by an adequate period of normal circulation in a nerve, before this nerve becomes the seat of changes felt as paræsthesiæ.

Although these changes are apparently initiated within a few seconds of release of the circulation, they progress relatively slowly, for there is a striking and constant delay before the paræsthesiæ actually do begin. Kugelberg's studies show that the excitability of human motor nerves to electrical stimuli is greatly increased at about the time when paræsthesiæ are at their height ; it is likely that the appearance of spontaneous impulses felt as paræsthesiæ is directly related to a similar increase in excitability in the sensory nerves.

A clear distinction should be drawn between the delay before the appearance of paræsthesiæ, and the time taken for anæsthesia to recover, after the return of the circulation to an ischæmic limb. The two events are independent. In the first place, the usual delay which precedes the paræsthesiæ can be observed after periods of ischæmia so brief that peripheral sensation has never been demonstrably affected. Further, in experiments of longer duration, sensation in the territory of a given nerve may fully recover many seconds before the paræsthesiæ are first felt in that area. The nerve regains its ability to conduct before it enters the phase of increased excitability. For many hours after this phase has passed and paræsthesiæ have ceased, the nerve still remains in an abnormal state, although sensation in its territory is apparently perfectly normal. During this period, as Lewis, Pickering, and Rothschild have described, further arrest of the circulation leads to the unusually early onset of anæsthesiæ and paralysis ; but it may also be observed that ischæmic and post-ischæmic paræsthesiæ are much reduced in severity. We have already pointed out that diminution of the ischæmic paræsthesia is a most sensitive indicator of these residual effects in a limb ; by noting its absence, we have found on many occasions that the effect of compression of the arm for thirty minutes lasts fully twenty-four hours. The nature of this remarkably persistent change in the nerve is at present unknown.

Summary

Certain forms of paræsthesiæ felt on release of the circulation to an ischæmic limb have been investigated.

The various paræsthesiæ are defined and described, and methods of producing them separately are given. An account is given of the more important factors modifying the paræsthesiæ.

Evidence is presented which shows that the nerve impulses felt as paræsthesiæ arise in the nerves recovering from ischæmia, and not in the end-organs.

It is shown that the nerve fibres concerned are those which normally subserve the sensations of touch, pressure, and movement. Pain, temperature, and sympathetic fibres play no part.

Evidence is given which shows that the paræsthesiæ are conducted in the posterior columns of the cord, and not in the antero-lateral columns.

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